UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported):

October 13, 2025

Denali Therapeutics Inc.

(Exact name of registrant as specified in its charter)

Delaware	001-38311	46-3872213
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

161 Oyster Point Blvd.
South San Francisco, California 94080
(Address of principal executive offices, including zip code)

(650) 866-8547
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former address, if changed since last reports)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol (s)	Name of each exchange on which registered
Common Stock, par value $0.01 per share	DNLI	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On October 13, 2025, Denali Therapeutics Inc. issued a press release announcing that the U.S. Food and Drug Administration (FDA) has extended the Prescription Drug User Fee Act (PDUFA) date for the Company's Biologics License Application (BLA) seeking accelerated approval of tividenofusp alfa for the treatment of mucopolysaccharidosis type II (MPS II), also known as Hunter syndrome. The FDA extended the PDUFA action date from January 5, 2026 to April 5, 2026 to allow for the review of updated clinical pharmacological information which was submitted by the Company and classified as a Major Amendment to Denali's BLA. A copy of the press release is attached hereto as Exhibit 99.1 and incorporated herein by reference.

The information furnished in this Item 7.01 and Item 9.01 (including Exhibit 99.1) shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press release dated October 13, 2025.
104	Cover Page Interactive Data File (formatted as Inline XBRL)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

DENALI THERAPEUTICS INC.

Date: October 14, 2025

By: /s/ Alexander O. Schuth
Alexander O. Schuth, M.D.
Chief Operating and Financial Officer

Denali Therapeutics Announces FDA Review Extension of BLA for Tividenofusp Alfa for the Treatment of MPS II (Hunter Syndrome)

SOUTH SAN FRANCISCO, Calif., Oct. 13, 2025 – Denali Therapeutics Inc. (Nasdaq: DNLI) today announced that the U.S. Food and Drug Administration (FDA) has extended its review timeline of the Biologics License Application (BLA) seeking accelerated approval of tividenofusp alfa for the treatment of mucopolysaccharidosis type II (MPS II), also known as Hunter syndrome. The Prescription Drug User Fee Act (PDUFA) target date has been extended from January 5, 2026, to April 5, 2026.

The extension follows Denali's submission of updated clinical pharmacology information in response to an information request from the FDA as part of the standard review process and is not related to efficacy, safety or biomarkers. The FDA classified the submission as a Major Amendment (MA) to the BLA, which, per FDA regulations, extends the review by three months. No additional data were requested by the FDA in the MA letter. Denali believes that the updated information submitted in the amendment does not affect the clinical pharmacology or benefit-risk conclusions of the BLA.

"We appreciate the FDA's continued collaboration throughout the review process," said Ryan Watts, Ph.D., Chief Executive Officer of Denali Therapeutics. "We continue to prepare for the potential approval and commercial launch of tividenofusp alfa. We feel the urgency to deliver for the MPS community, and we are committed to working together with regulators, physicians, and advocates to bring this important therapy to individuals and families living with Hunter syndrome."

About Tividenofusp Alfa

Tividenofusp alfa (DNL310) is composed of the iduronate 2-sulfatase (IDS) enzyme fused to Denali's proprietary TransportVehicle™ (TV) platform, designed to deliver IDS into the brain and the body, with the goal of addressing behavioral, cognitive and physical symptoms of Hunter syndrome (MPS II). The U.S. Food and Drug Administration has granted Fast Track and Breakthrough Therapy designations to tividenofusp alfa for development in the treatment of MPS II. The European Medicines Agency has granted Priority Medicines designation to tividenofusp alfa.

The Phase 2/3 COMPASS study is enrolling participants with MPS II in North America, South America and Europe to support global approval. Participants are randomized 2:1 to receive either tividenofusp alfa or idursulfase, respectively. More information about the COMPASS study can be found here.

Tividenofusp alfa is an investigational therapeutic and has not been approved for use by any Health Authority.

About Hunter Syndrome (MPS II)

Hunter syndrome, also known as MPS II, is a rare genetic lysosomal storage disease caused by mutations in the iduronate-2-sulfatase (IDS) gene. This results in a deficiency of the IDS enzyme, which is responsible for breaking down glycosaminoglycans (GAGs) such as heparan sulfate and dermatan sulfate. The accumulation of GAGs leads to progressive damage in multiple organs and tissues, including the brain. Symptoms of Hunter syndrome include developmental delays, cognitive decline, behavioral abnormalities and physical complications such as joint stiffness, hearing loss and organ dysfunction. Current standard-of-care enzyme replacement therapies do not cross the blood-brain barrier and therefore do not address the neurological symptoms of the disease. There is a significant unmet need for therapies that address both the central nervous system (CNS) and peripheral manifestations of Hunter syndrome.

About Denali Therapeutics

Denali Therapeutics is a biotechnology company developing a broad portfolio of product candidates engineered to cross the blood-brain barrier (BBB) for the treatment of neurodegenerative diseases and lysosomal storage diseases. Denali pursues new treatments by rigorously assessing genetically validated targets, engineering delivery across the BBB, and guiding development through biomarkers that demonstrate target and pathway engagement. Denali is based in South San Francisco. For additional information, please visit www.denalitherapeutics.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements expressed or implied in this press release include, plans, timelines and expectations relating to tividenofusp alfa, including the timing of the PDUFA action date, the likelihood of regulatory approval, expectations regarding the adequacy of clinical data to support the BLA, and the timing and likelihood of commercial launch; expectations for ongoing communications with the FDA; and statements made by Denali's Chief Executive Officer. Actual results may differ materially from those expressed or implied by these forward-looking statements due to a variety of risks and uncertainties. These include, but are not limited to, risks that the PDUFA action date may be extended and the FDA may ultimately determine not to approve the BLA in its present form or at all; risks arising from adverse economic conditions and their impact on Denali's business and operations; the possibility of events or changes that could lead to the termination of Denali's collaboration agreements; challenges associated with Denali's transition to a late-stage clinical drug development company; the ability of Denali and its collaborators to complete the development and, if approved, the commercialization of product candidates; difficulties in patient enrollment for ongoing and future clinical trials; reliance on third-party manufacturers and suppliers for clinical trial materials; dependence on the successful development of Denali's blood-brain barrier platform technology and related programs; potential delays or failures in meeting expected clinical trial timelines; the risk that promising preclinical profiles may not be replicated in clinical settings; discrepancies between preclinical, early-stage, or preliminary clinical results and outcomes from later-stage trials; the occurrence of significant adverse events or other undesirable side effects; and the uncertainty surrounding regulatory approvals required for commercialization; Denali's ability to advance a pipeline of product candidates or develop commercially successful products; developments relating to Denali's competitors and its industry, including competing product candidates and therapies; Denali's ability to obtain, maintain, or protect intellectual property rights related to its product candidates; implementation of Denali's strategic plans for its business, product candidates, and blood-brain barrier platform technology; Denali's ability to obtain additional capital to finance its operations, as needed; Denali's ability to accurately forecast future financial results in the current environment; and other risks and uncertainties, including those described in Denali's most recent Annual and Quarterly Reports on Forms 10-K and 10-Q filed with the Securities and Exchange Commission (SEC) on February 27, 2025 and August 11, 2025, respectively, and Denali's future reports to be filed with the SEC. Denali's product candidates are investigational, and their safety and efficacy profiles have not yet been established. No Denali product candidates have been approved by any Health Authority for any use. Denali does not undertake any obligation to update or revise any forward-looking statements, to conform these statements to actual results or to make changes in Denali's expectations, except as required by law.

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